Physiology of Aging

Background
1. Definition
   - Aging - process that converts healthy adults into frail ones with diminished reserves in most physiologic systems and an exponentially increasing vulnerability to disease and death
2. General information
   - Degree of altered physiology varies widely
   - Degree of physiologic reserve varies widely
   - Physical conditioning can greatly affect some changes seen with age, especially cardiovascular ones
   - Acute illness may manifest clinically in the organ that has the least physiologic reserve
     - Worsening incontinence during a lung infection
     - Fall during a UTI
     - Confusion as the presenting sign of an MI

Neurology
1. Pearls
   - Memory loss that significantly affects function is not a part of normal aging
2. Normal changes and clinical implications
   - Decrease in brain size and weight
     - Higher risk of developing an subdural hematoma
   - Decreased number and size of neurons
   - Changes in neurotransmitter numbers and deficits in various aspects of cholinergic, dopamine, norepinephrine and serotonin signaling
     - Increased sensitivity to extrapyramidal effects of dopamine receptor antagonist drugs
     - Increased sensitivity to anticholinergic and sedating drugs
     - Increased risk of depression
   - Decreased stage IV sleep, increase stage I sleep and increased in night time wakening
     - Increase in perceived or real sleeping disorders
   - Slowed processing of information and sometimes decreased recall, particularly of short term memory

Pulmonology
1. Pearls
   - In general, changes in the pulmonary system do not have a large clinical impact, but do make elderly patients more susceptible to disease and the long-term effects of smoking
2. Normal changes and clinical implications
   - Decreased cough and mucociliary clearance
   - Reduction of airway size
   - More shallow alveolar sacs
   - Intercostal muscle atrophy, reduced diaphragmatic strength (25%)
   - Lower maximal expiratory flows: (FEV1, FEV1/FVC, FEF 75%)
   - Increased FRC and RV, lower VC, but stable TLC
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- Lower diffusing capacity
  - Lower pO2 and SpO2, no change in PCO2
- Lower respiratory muscle strength and endurance
- Stiffer chest wall
- Increased lung tissue compliance (loss of recoil)
  - Increased incidence of air trapping
- Reduced respiratory drive during hypoxia, hypercarbia
  - Decreased ventilatory response during heart failure, pneumonia or COPD exacerbation
- Increased airway reactivity

**Cardiology**

1. Pearls
   - Compensatory mechanisms are employed by the aging heart to maintain normal heart rate, EF, and cardiac output at rest, but are therefore less available during stress and illness
   - Changes in physical activity can radically change cardiovascular function

2. Normal changes and clinical implications
   - Decreased elasticity and increased stiffness of arterial system
     - Increased afterload on LV
     - Increased SBP and LVH
     - Slowed ventricular relaxation, decreased diastolic function
     - Increased pulse pressure
   - Loss of cardiac myocytes and hypertrophy of remaining myocytes
     - Together with increased LV afterload results in LVH
     - Decreased ability to adapt after hypoxic stress
   - LVH, LAH, and increased fibrosis
     - Decreased left ventricular compliance, decreasing diastolic function
     - Almost universal S4
   - Increased atrial and mitral valve thickness due to calcification and fibrosis
     - Higher risk of clinically relevant valvular disease
   - Less compliant vasculature
     - Increases in volume lead to increases in blood pressure
   - Compromise of baroreceptivity
     - Increased sensitivity to the physiologic effects of prolonged bed rest, dehydration, cardiovascular drugs and illness resulting in a higher risk of falls, orthostatic hypotension, dizziness and other symptoms
   - Decreased VO2 max with exercise
   - Decreased maximal heart rate, stroke volume, and cardiac output
     - Fewer reserves left to respond to additional acute stress
   - Decrease heart responsiveness to both parasympathetic and sympathetic nervous system
     - Decreased heart rate variability during stress and illness
   - Dropout of atrial pacemaker cells
     - Decrease of intrinsic heart rate
   - Decreased nitrous oxide production
Gastroenterology

1. Pearls
   o Though physiologic changes of aging may affect gastrointestinal function, most gastrointestinal symptoms and signs are due to pathologic conditions and the drugs we use to treat them

2. Normal changes and clinical implications
   o Recession of gums, decreased saliva production and coordination of swallowing
     ▪ Increased risk of dysphagia, aspiration, weight loss and malnutrition
   o Decreased gastric mucosal cytoprotection
     ▪ Increased risk of ulceration in response to stress/meds
   o Decreased esophageal acid clearance
     ▪ Increased incidence of GERD symptoms
   o Possible impaired GI tract mucosal immunity and reduced gastric acid
     ▪ Increased susceptibility to infections that enter the body via GI tract
   o Colonic slowing
     ▪ Increased rates of constipation
     ▪ In combination with decreased tensile strength of colonic mucosa, increased risk of diverticulosis
     ▪ Possible increased exposure to carcinogens
   o Reduced CYP3A activity (most common cytochrome of P450 system)
     ▪ Impaired metabolism of drugs including Ca channel blockers, cholesterol lowering agents, benzodiazepines, non-sedating antihistamines, macrolide antibiotics and immunosuppressant agents
   o Reduced hepatic blood flow, size, and perfusion
     ▪ Very little clinical impact until total hepatic functional reserve reduced beyond 70%
   o Preserved pancreatic function

Nephrology

1. Pearls
   o There is a wide range in the rate and extent of loss of kidney function between individuals
   o Cockcroft-Gault should be used to estimate renal function in the elderly, recognizing that a "normal range" creatinine may still represent significant functional impairment
   o Renally excreted drugs should be dosed appropriately
   o Special care should be used when using renally toxic drugs including NSAIDs and radiocontrast
   o Reduction of BP below 125/75, lipid control, diabetic control, and use of ACE/ARBs should be instituted in patients with impaired renal function

2. Normal changes
   o Spontaneous progressive decline in renal function with the number of nephrons declining after the 4th decade
   o Decreased renal blood flow
   o Thickening of basement membrane and mesangial expansion
   o Focal glomerulosclerosis starting in the 5th decade
   o Decreased concentrating abilities of the kidneys
3. Clinical implications
   - Decreased renal reserves
   - Decreased ability to respond to salt or water load/deficits
   - Increased sensitivity to nephrotoxic drugs and acute ischemic renal failure

**Immunology**
1. Pearls
   - Greatest contribution to increased risk of infection in elderly is the increased incidence of comorbid conditions
   - Nutritional status is a major confounder in studying the elderly immune system, especially protein energy malnutrition and vitamin deficiencies
   - Serious infections may present with only non-specific decline
2. Normal changes and clinical implications
   - Immune senescence:
     - Dysregulation of immune responses at several levels
     - Involution of thymus and production of thymic hormones
     - Reduction of T-cell immunity
     - Reduction in B-cell immunity
     - Changes in cytokine level and function
     - Reduction in adaptive immune responses (T-cell function)
     - Up-regulated inflammatory response
     - Reduced natural killer cell activity
     - Possibly reduced neutrophil function
     - Decreased response to endogenous pyrogens and lower mean baseline body temperature
       - Decreased likelihood of mounting a fever during illness
       - Possibility of decreasing temperature during acute illness
     - Increase in autoantibodies
     - Undetermined clinical significance
     - Decreased response to vaccinations
     - Decreased ability to mount an elevated WBC during bacterial infection
     - Increased susceptibility to infections and reinfections such as TB, shingles

**Musculoskeletal System And Integument**
1. Pearls
   - Most pain not from arthritis but rather by problems with tendons, bursae, muscles, connective tissue, and nerves
   - It is often difficult to separate aging from disuse and from disease
2. Normal changes and clinical implications
   - Decreased muscle mass and increased total body fat
     - Decreased total body water and increased sensitivity to water soluble drugs
     - Increased half life of fat soluble drugs
     - Increased risk of falls
   - Accumulation of modified/degraded extracellular matrix components
   - Increased collagen cross-linking
   - Decreased number of stem cells to replace lost cells
   - Decreased mitogenic response to injury
o Decreased synthetic capacity in response to growth factor stimulation
  ▪ Increased incidence of osteoarthritis
  ▪ Increased incidence of osteoporosis
o Loss of interdigitations between dermis and epidermis
  ▪ Increased risk of skin tears
o Decreased vascular supply to skin, decreased peripheral vasoconstriction to cold
  ▪ Altered thermoregulation with increased risk of both hypo- and hyperthermia
  ▪ Altered transdermal drug absorption
o Decreased immune cells in the skin
  ▪ Increased risk of skin infections
o Decline in vit D activation in skin
  ▪ Increased risk of low vit D levels
o Decreased ability to sweat
  ▪ Increased risk of hyperthermia
o Decreased shivering response
  ▪ Increased risk of hypothermia

**Endocrine**
1. Impaired homeostatic regulation may only manifest during stress
2. Nonspecific or atypical presentation of endocrine disease is common in the elderly
3. Normal ranges for healthy older people are not available for most laboratory tests
4. Normal changes and clinical implications
5. Glucose control
   o Little/no change in fasting blood sugar
   o Impaired response to glucose challenge
   o Impaired glucose tolerance
     ▪ Increased risk of diabetes
6. Adrenal function
   o Decrease in basal serum aldosterone levels (30% by age 80)
     ▪ Increased risk of hyperkalemia
7. Thyroid and parathyroid function
   o Reduced T4 secretion & decreased T4 clearance
     ▪ Reduced thyroid replacement requirements with age (as much as 1/3 lower)
     ▪ Increased incidence in hyper and hypothyroidism
   o No change in T3, although during illness may get decreased T4 to T3 conversion
   o Unchanged TSH
   o Increased parathyroid hormone (30% higher between ages 30 to 80)
   o Bone resorption favored over bone formation
     ▪ Increased risk of osteoporosis
8. Hormones involved in volume control
   o Higher ADH secretion to osmoreceptor stimuli
     ▪ Predisposition to hyponatremia
   o Higher atrial natriuretic hormone levels
   o Decreased baroreceptor ADH responsiveness to hypotension and hypovolemia and decreased renal responsiveness to ADH
o Decreased thirst sensation
  ▪ Increased susceptibility to volume depletion
9. Other hormone changes
  o Decreased DHEA levels (only 10-20% of young adults levels produced by age 80)
    ▪ Decreased bone mineral density
  o Decreased testosterone secretion and increased sex hormone binding proteins
  o Menopause results in decreased estrogen, progesterone, and androgens
  o Decreased growth hormone secretion (50% by age 80)
  o Decreased melatonin production after childhood
    ▪ Unknown significance
  o Inability to increase intestinal absorption of vitamin D with decreased intake
    ▪ Higher prevalence of vitamin D deficiency

Genitourinary System
1. Normal changes and clinical implications
  o Increased bacterial adherence to mucosa
  o Increased urethral colonization by gram negative bacteria
    ▪ Increased incidence of urinary tract infections
  o Decreased blood flow
    ▪ Increased time to orgasm
    ▪ Increased incidence of erectile dysfunction
  o Increased size of prostate
    ▪ Increased incidence of symptomatic prostatic hypertrophy

Sensory Systems
1. Normal changes and clinical implications
2. Vision
  o Yellowing and opacification of lens
    ▪ Altered color perception
  o Decrease in light to dark adaptation
  o Decreased lens elasticity
    ▪ Increased distance of focusing
  o Decreased contrast sensitivity
  o Increased sensitivity to glare
3. Taste and smell
  o Decreased sensitivity to taste and impaired smell
    ▪ May result in decreased interest in eating
    ▪ Increased risk of weight loss and malnutrition
    ▪ Increased risk of food poisoning
4. Hearing
  o Stiffening, thickening, and calcification of multiple parts of the middle and inner ear
  o Decreased cochlear neurons
  o Decreased hair cells
    ▪ Decreased hearing
References

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